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IN THE UNITED STATES DISTRICT COURT FOR THE DISTRICT OF UTAH,

CENTRAL DIVISION

NUTRACEUTICAL CORPORATION, et al.,	)	
Plaintiffs,	)	**MEMORANDUM OF POINTS AND AUTHORITIES IN SUPPORT OF PLAINTIFFS' MOTION FOR SUMMARY JUDGMENT**
v.	)	
ANDREW VON ESCHENBACH, M.D., Acting Commissioner of the U.S. Food and Drug Administration, et al.,	)	**(Oral Argument Requested)**
Defendants.	)	Case No. 2:04-CV-00409-PGC

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Plaintiffs Nutraceutical Corporation and Solaray, Inc. (collectively "Nutraceutical") are entitled to summary judgment in their favor on claims 3 and 4 of their Complaint. There are no disputed issues of material fact concerning those causes of action and the legal issues, as a matter of law, must be decided in Nutraceutical's favor.

The legal issues involved in those counts are:

(1) 3rd Claim: Whether the FDA violated 5 U.S.C. § 553(b)-(d) of the Administrative Procedure Act when it failed to publish notice in the Federal Register of, and provide the regulated class, including Nutraceutical, an opportunity to comment upon, use of a risk-benefit standard to determine the existence of dietary supplement adulteration, and

(2) 4th Claim: Whether the FDA violated 5 U.S.C. § 706 of the Administrative Procedure Act by engaging in arbitrary and capricious agency action when in its Final Rule it simultaneously banned from the market all quantities of ephedrine alkaloids in a dietary supplement not used in traditional Asian medicine but exempted from its ban every quantity of ephedrine alkaloids in conventional foods and every quantity of ephedrine alkaloids in traditional Asian medicine available without a prescription.

Plaintiffs are entitled to summary judgment on their third claim because, as a matter of law, Defendants violated the Administrative Procedure Act (APA) requirement that FDA publish in the Federal Register notice and provide an opportunity for comment when they *sua sponte* adopted in their 2004 Final Rule a legislative rule applicable in all dietary supplement adulteration cases (the 2004 Final Rule risk-benefit comparison standard for determining the existence of adulteration).

Plaintiffs are entitled to summary judgment on their fourth claim because, as a matter of law, Defendants violated the APA requirement that FDA not take action that is arbitrary and capricious when FDA pronounced ephedrine alkaloids down to a molecule

adulterated in dietary supplements but entirely exempt from the adulteration ruling in foods (teas) and in traditional Asian medicines sold without a prescription.

This Court, therefore, should: (1) declare the Final Rule invalid in violation of 5 U.S.C. §§ 553 and 706; (2) remand the matter to FDA for further rulemaking consistent with the Court's opinion; and (3) enjoin the Defendants from enforcing the Final Rule pending completion of that rulemaking.

STATEMENT OF UNDISPUTED MATERIAL FACTS ENTITLING NUTRACEUTICAL TO SUMMARY JUDGMENT

In support of Plaintiffs' motion, and pursuant to DUCivR 56-1(b), Plaintiffs present these materials facts for which there is no genuine issue and which entitle Plaintiffs to summary judgment on their 3rd and 4th claims as a matter of law.

1. The *Ephedra* genus of plants, including raw crushed *Ephedra sinica* herb, has been used as a tea – a food – for thousands of years. [See, e.g., Food and Drug Administration's (FDA's) Briefing Materials for Food Products Containing Ephedrine Alkaloids at 5 (October 11-12, 1995); 95N-0304, Vol. 39, Ref. 1 (attached as **Exhibit J**)]

2. Since at least 1988, Solaray (purchased by Nutraceutical in 1993) has manufactured and sold a gelatin capsule containing raw crushed *Ephedra sinica* herb as a dietary supplement. [Nutraceutical Corp.'s Comments at 3 (Apr. 7, 2003), 95N-0304, Vol. 326, EC-1452 (attached as **Exhibit C**)]

3. From 1993 until February 11, 2004 when FDA banned dietary supplements containing ephedrine alkaloids, Nutraceutical marketed a dietary supplement comprised of raw crushed *Ephedra sinica* herb in a gelatin capsule. ["Final Rule Declaring Dietary Supplements Containing Ephedrine Alkaloids Adulterated Because They Present an Unreasonable Risk; Final Rule," 69 Fed. Reg. 6788 (February

11, 2004 (hereinafter "Final Rule")] At the time of the ban, and for years prior to that date, Nutraceutical's product contained 375 mg of raw crushed *Ephedra sinica* herb per capsule. Each capsule yielded a dose of 5 mgs or less of ephedrine alkaloids. Directions for use on the label recommended that consumers "take one capsule no more than two times a day with meals or a glass of water," yielding a daily dose of ephedrine alkaloids of 10 mgs or less. [The label is attached as Exhibit A]

4. The raw crushed *Ephedra sinica* herb in Nutraceutical's gelatin capsule dietary supplement is precisely the same herb used in ephedra tea. [Compare the label attached at **Exhibit** A with FDA's Briefing Materials for Food Products Containing Ephedrine Alkaloids at 5 (Oct. 11-12, 1995), 95N-0304, Vol. 39, Ref. 1 (attached as **Exhibit J**) ("Ma Huang is a traditional Chinese medicine derived from the above-ground parts of several plant species belonging to the genus *Ephedra*. The term Ma huang refers to *Ephedra sinica* Stapf, *E. equistestina* Bunge, *E. intermedia* var *tibetica* Stapf, and *E. distachya* L")] FDA exempted all food containing ephedrine alkaloids, other than dietary supplements, from its ephedrine alkaloid ban.

5. Quantities of ephedrine alkaloids in ephedra tea range from 15 to 30 mgs or more per serving with tea drinkers often consuming multiple glasses per sitting. [FDA's Briefing Materials for Food Products Containing Ephedrine Alkaloids at 5 (Oct. 11-12, 1995), 95N-0304, Vol. 39, Ref. 1 (attached as **Exhibit J**)]

6. On June 4, 1997, FDA first published a notice of proposed rulemaking entitled "Dietary Supplements Containing Ephedrine Alkaloids." [62 Fed. Reg. 30678 (June 4, 1997) ("1997 Proposed Rule")] In it, FDA proposed the following dose specific limits and warnings on dietary supplements containing ephedrine alkaloids:

a. A dietary supplement would be adulterated and thus illegal to sell if it contained 8 mg or more of ephedrine alkaloids per serving or if its labeling recommended conditions of use resulting in an intake of 8 mg or more in a 6 hour period or a total daily dose of 24 mg or more;

b. The label on all dietary supplements containing ephedrine alkaloids must state that the product should not be used for more than seven days;

c. Dietary supplements containing ephedrine alkaloids could not be combined with certain other ingredients with a known stimulant effect;

d. The labeling for dietary supplements containing ephedrine alkaloids could not include claims for weight loss or body building that required long-term intake to achieve the purported effect;

e. The labeling for dietary supplements containing ephedrine alkaloids must include a warning that taking more than the recommended serving may result in serious adverse health effects. It must also warn consumers with certain diseases to consult a health professional before use and to stop use if he or she has certain signs or symptoms.

7. In the 1997 Proposed Rule, FDA considered adverse event and pharmacologic data concerning potential illness or injury (i.e., risks) caused by specific dose levels of ephedrine alkaloids. [62 Fed. Reg. at 30678-30679, 30680-30691]

8. In the 1997 Proposed Rule, FDA performed a dose specific analysis, finding evidence of clinically serious adverse events present at intake levels above 10 mg ephedrine alkaloids *per serving* but, in this 1997 Proposed Rule, FDA recommended *per*

serving levels "as low as 8 to 9 mg ephedrine alkaloids." [62 Fed. Reg. 30678] FDA wrote:

> Given the available evidence, it is difficult to ascertain whether there is a threshold level of ephedrine alkaloids below which the general population and susceptible individuals will not experience serious adverse events. The shape of an intake-response curve for any particular adverse effect related to ephedrine alkaloid intake is not known. In the absence of data that allow a systematic evaluation of intakes of ephedrine and other related alkaloids below 10 mg per serving, it is not possible to adequately define or describe the potential risks and at-risk groups from ephedrine alkaloids. However, the available data, including the AER's and the known physiological and pharmacological effects of ephedrine, provide convincing evidence that clinically serious adverse events will occur at intake levels above 10 mgs ephedrine alkaloids per serving.

[62 Fed. Reg. at 30693]

9. Nutraceutical's dietary supplement contained 5 mg or less of ephedrine alkaloids *per serving*. [Nutraceutical Corp.'s Comments at 3 (Apr. 7, 2003), 95N-0304, Vol. 326, EC-1452 (attached as **Exhibit C**)]

10. In the 1997 Proposed Rule, FDA did not compare ephedrine alkaloid risks with health benefits in determining the existence of adulteration. Rather, FDA determined dietary supplement adulteration under what it described as its then extant "policy" of identifying the dose level at which "food ingredients," including ephedrine alkaloids, present a risk of illness or injury and finding adulteration at that dose level and above, reasoning:

> Given the AER's, the case reports in the scientific literature, controlled clinical trials, published reports of adverse effects with traditional uses of ephedrine alkaloid-containing botanicals, and other data, it is apparent that there are serious and well-documented public health risks attendant to the use of ephedrine alkaloids in marketed dietary supplement products, and that the agency needs to propose actions to address these risks.
>
> Over the years, FDA has employed a variety of strategies in addressing food ingredients that created significant public health risks. In cases

> where small subpopulations have faced serious, even potentially deadly, risks because of ingredients with allergic potential (e.g., nuts and shellfish), FDA has required that the presence of the allergen be declared on the food label so that consumers who are at risk can avoid products that contain the problem ingredient (§ 101.4 (21 CFR 101.4)). In other cases where a food or food ingredient has presented special risks to consumers under certain use conditions, the agency has required warning label statements to ensure that consumers are alerted to the potential health hazards associated with use of the product. For example, FDA has required a special warning statement to appear on the label of protein products intended for use in weight reduction, stating in part that very low calorie protein diets may cause serious illness or death (§ 101.17(d) (21 CFR 101.17(d))). In other cases, e.g., the proposed regulations for poisonings in young children because of high intakes of iron-containing dietary supplements, the agency was concerned that, for high potency products, warning labels alone would not be effective in preventing serious harm. Therefore, the agency has decided to require, at least in some cases, warning labels plus special packaging requirements to reduce the risk of serious harm (Ref. 150).
>
> In other cases, where a substance contained in a food may be harmful to health, it has been the agency's policy to define a level at which the harmful substance may render the food adulterated. For example, to address the public health problem of histamine poisoning associated with the consumption of certain fish, the agency issued guidance on the level of histamine at which FDA is likely to take action against the fish because it is adulterated (Ref. 151). . . .

[62 Fed. Reg. at 30692]

11. In its 1997 Proposed Rule, FDA -- in analyzing adulteration -- considered whether ephedrine alkaloids were "injurious to health" at a specific quantitative amount (from the Adulterated Food "injurious to health" provision, 21 U.S.C. § 342(a)(1)) and considered whether ephedrine alkaloids presented a "significant and unreasonable" risk of illness or injury. FDA in its 1997 Proposed Rule, unlike in its 2004 Final Rule, did not interpret "significant" and "unreasonable" disjunctively (from the FDCA Adulterated Food "significant or unreasonable risk" provision, 21 U.S.C. § 342(f)(1) (emphasis added)), and did not provide a definition for "unreasonable" as begetting a standard

comparing risks with benefits. Rather, in the 1997 Proposed Rule, FDA read "significant" and "unreasonable" conjunctively, gave no separate definition for "unreasonable," and articulated no standard for adulteration that compared risks with benefits. FDA wrote:

> Based on the available evidence and the likely sources of measurement error around estimated intake levels, the agency tentatively concludes that the use of dietary supplements containing 8 mg or more ephedrine alkaloids per serving may render the dietary supplement injurious to health. The agency also tentatively concludes that consumption of dietary supplements that contain this level or more of ephedrine alkaloids presents a significant and unreasonable risk of illness or injury under the conditions of use recommended or suggested in the labeling or under ordinary conditions of use, and that, therefore, products that contain this or higher levels of ephedrine alkaloids are adulterated.

[62 Fed. Reg. at 30693]

12. In its 1997 Proposed Rule, FDA recited in a paragraph immediately following the one quoted in paragraph 11 above that it acted pursuant to Section 402(a)(1) of the Food Drug and Cosmetic Act ("FDCA") (i.e., 21 U.S.C. § 342(a)(1), the "injurious to health" provision) as well as Section 402 (f)(1)(A) of the FDCA (i.e., 21 U.S.C. § 342(f)(1)(A), the "significant or unreasonable risk" provision), interpreting them as a harmonious whole:

> Under section 402(a)(1) of the act, a food, including a dietary supplement, is adulterated if it bears or contains any added poisonous or deleterious substance that may render it injurious to health. Section 402(f)(1)(A) of the act provides that a dietary supplement is adulterated if it, or one of its ingredients, poses a significant or unreasonable risk of injury or illness when used as directed or under ordinary conditions of use. Under section 701(a) of the act, FDA has authority to issue regulations for the efficient enforcement of the act. These sections authorize FDA to issue a regulation that establishes a level of ephedrine alkaloids that, the available evidence makes clear, will render a dietary supplement adulterated as a matter of law.

[62 Fed. Reg. at 30693]

13. In its 1997 Proposed Rule, FDA recited in a paragraph immediately following the one quoted in paragraph 12 above (wherein the statutory language "significant **or** unreasonable risk" is recited), its conclusion that ephedrine alkaloids in *servings* of 8 mg and above present a "significant **and** unreasonable risk" and are adulterated at that level and above, again omitting any comparison of risk with benefit and giving no independent meaning to the term "unreasonable risk" in the statute:

> Eight mg per serving and above represent levels at which the presence of ephedrine alkaloids in a dietary supplement may render the product injurious to health and presents a significant **and** unreasonable risk.

[62 Fed. Reg. at 30693 (emphasis added)]

14. Plaintiffs filed comments in response to the 1997 Proposed Rule on December 2, 1997. Plaintiffs challenged the legal authority and evidentiary basis for FDA's proposed limitations on the sale of dietary supplements containing ephedrine alkaloids. [Those comments are attached as **Exhibit B**]

15. On April 3, 2000, Defendants published a modification (hereinafter the "2000 Modification"); Defendants withdrew the following specific parts of the 1997 Proposed Rule, leaving all other parts intact:

a. That a supplement is adulterated if it contains 8 mg or more of ephedrine alkaloids per serving or if its labeling recommends conditions of use that would result in an intake of 8 mg or more in a 6 hour period or a total daily intake of 24 mg or more;

b. The analytical method for determining amounts present;

c. The label statement, "Do not use this product more than 7 days;"

d. The prohibition on labeling claims encouraging long-term intake;

e. The proposed warning for short term use.

[65 Fed. Reg. 17474, 17476 (Apr. 3, 2000)]

16. In the 2000 Modification, FDA withdrew parts of its rule in the face of Government Accountability Office (GAO) criticism of FDA's failure to rely on adequate scientific evidence to support its conclusions. [65 Fed. Reg. at 17474-17475]

17. In the 2000 Modification, FDA referred to risks associated with consumption of dietary supplements containing ephedrine alkaloids and solicited more comment on the "safety" of ephedrine alkaloids. [65 Fed. Reg. at 17476]

18. In the 2000 Modification, FDA neither withdrew the adulteration standard nor presented an adulteration standard that differed from the one described in its 1997 Proposed Rule. In the 2000 Modification, FDA did not invite comment on whether FDA should adopt a standard comparing ephedrine alkaloid risks with ephedrine alkaloid health benefits as the basis for a finding of adulteration.

19. On March 5, 2003, FDA published a notice in the Federal Register reopening the comment period for the 1997 Proposed Rule ("2003 Reopened Proposed Rule"). The notice sought comment on the same notice statement proposed in its 1997 Proposed Rule at 62 Fed. Reg. 30678. The notice also sought comment on whether, in light of data FDA received since the 1997 Proposed Rule, FDA should find that dietary supplements containing ephedrine alkaloids were adulterated under the statute, i.e., presented a "significant or unreasonable risk of illness or injury under conditions of use recommended or suggested in labeling, or if no conditions of use are suggested or recommended in the labeling, under ordinary conditions of use." [68 Fed. Reg. 10417 (March 5, 2003)]

20. In its 2003 Reopened Proposed Rule, FDA did not articulate a position concerning the meaning of adulteration that differed from the one expressed in its 1997 Proposed Rule. [See supra at paragraphs 10-13] It did not state the view that the term "unreasonable" in 21 U.S.C. 342(f)(1) would be interpreted to mean a risk-benefit comparison standard, and it did not state that the term "significant" in the statutory section would not be given a conjunctive meaning with "unreasonable" but would be given no meaning at all. [Id.]

21. In its 2003 Reopened Proposed Rule, FDA did not propose or solicit comment on any new standard for determining dietary supplement adulteration. FDA did not propose or solicit comment on a comparison of dietary supplement risks with benefits for determining adulteration. FDA did not propose or solicit comment on whether the existing policy for determining adulteration stated in the 1997 Proposed Rule, which included an assessment of the dose level "injurious to health" and that presented a "significant and unreasonable risk," should be replaced with any other standard for determining the existence of adulteration.

22. Nutraceutical filed comments in response to the 2003 Reopened Proposed Rule on April 7, 2003. Plaintiffs requested that their product, containing 5 mg or less per serving of ephedrine alkaloids and 10 mg or less per daily dose of ephedrine alkaloids, be excepted from any final rule adopted by FDA because those low dose levels of ephedrine alkaloids had not been shown by scientific evidence to present a serious risk, and there had been no serious adverse events associated with those low dose levels. [The comments are attached as **Exhibit C**]

23. Nutraceutical filed additional comments on January 30, 2004, again requesting an exception. [The comments are attached as **Exhibit D**] Defendants did not respond to that request. Shortly thereafter, Nutraceutical Vice President, Legal, Stanley E. Soper along with Peter Barton Hutt, Esq., met with FDA's General Counsel, requested that the General Counsel grant an exception but again received no response.

24. On February 11, 2004, FDA published its Final Rule (effective April 12, 2004) banning all dietary supplements containing ephedrine alkaloids (including Nutraceutical's), without regard to the amount of ephedrine alkaloids present and without regard to whether ephedrine alkaloid content was naturally occurring or an extract having artificially elevated potency. ["Final Rule Declaring Dietary Supplements Containing Ephedrine Alkaloids Adulterated Because They Present an Unreasonable Risk," 69 Fed. Reg. 6787 (Feb. 11, 2004) ("2004 Final Rule")]

25. In its 2004 Final Rule, FDA announced: ". . . we are articulating a standard for unreasonable risk under 402(f)(1)(A) for the first time." [69 Fed. Reg. at 6794]

26. In its 2004 Final Rule, FDA stated: "We do not agree that we must define the . . . 'unreasonable risk' standard through regulation or guidance before taking action against dietary supplements containing ephedrine alkaloids based upon this standard." [69 Fed. Reg. at 6797]

27. Nutraceutical's Executive Vice President and Chief Operating Officer Jeffrey A. Hinrichs confirms that, from the content of the 1997 Proposed Rule, the 2000 Modification and the 2003 Reopened Proposed Rule, neither he nor any other Nutraceutical executive had any indication that FDA would promulgate a new standard

(one that would compare risk with health benefit) to determine the existence of dietary supplement adulteration. Moreover, he states that, if he had known FDA planned to articulate a standard of this kind for the first time, Nutraceutical would have filed comments providing FDA with insights on: (1) whether such a standard was appropriate or lawful for dietary supplements, which are regulated as a subclass of foods; (2) how, if the standard were adopted, health benefits and risks should be calculated; (3) how the two should be comparatively weighed; (4) how the treatment of a dietary ingredient in a dietary supplement should be harmonized with the treatment of that same ingredient in foods; and (5) how any ultimately adopted standard must ensure uniform protection of public health based on the substance (i.e., the ingredient itself), not on the form (i.e., presence in a conventional food rather than in a dietary supplement). In addition, he states neither he nor any other Nutraceutical executive anticipated that FDA would not include any analysis of the significance of risk or the effect of dose upon relative level of risk because of FDA's repeated emphasis on those very points in its 1997 Proposed Rule and failure to repudiate that method of analysis in FDA's 2000 Modification or 2003 Reopened Proposed Rule. Indeed, he states that the decision to modify and to reopen, rather than to close, the 1997 Proposed Rule and the failure to explain any difference in analysis gave him and other executives at Nutraceutical the distinct impression that FDA continued to propose the method of adulteration analysis offered in the 1997 Proposed Rule. That method of analysis (identifying harm from a dietary supplement at a specific dose level that is "injurious to health," 21 U.S.C. § 342(a)(1) and presents a "significant and unreasonable risk," 21 U.S.C. § 342(f)(1)(A)) included not only reference to the Adulterated Food section specifically concerning dietary supplements, 21 U.S.C. §

342(f)(1)(A), but also to the section specifically concerning foods, of which dietary supplements are statutorily defined as part, 21 U.S.C. 342(a)(1) (see paragraph 12 supra). [The Affidavit of Jeffrey A. Hinrichs is attached as **Exhibit E**]

28. In its 2004 Final Rule, FDA announced: "This regulation does not address the meaning of 'significant risk' or whether dietary supplements containing ephedrine alkaloids present a significant risk under section 402(f)(1)(A) of the Act." [69 Fed. Reg. at 6794]

29. In articulating a standard for "unreasonable risk," [69 Fed. Reg. 6823-6825], FDA concluded that such risk exists when the risk of illness or injury outweighs the benefits to health: " . . . unreasonable risk exists when a dietary supplement presents a risk to health, and there is no information substantiating a benefit sufficient to outweigh that risk." [69 Fed. Reg. at 6824]

30. In defining the standard, FDA made clear it considered a slight risk of illness or injury determinative that a dietary supplement was adulterated at every dose unless counterweighed by a significant health benefit: "In the absence of a sufficient benefit, the presence of even a relatively small risk of an important adverse health effect to a user may be unreasonable." [69 Fed. Reg. at 6788]

31. In defining the standard, FDA explained that any science based evidence of risk would suffice to prove risk in its newly declared test:

> The government's burden of proof for "unreasonable risk" can be met with any science-based evidence of risk and does not require a showing that the substance has actually caused harm in particular cases.

[69 Fed. Reg. at 6798]

> There is no requirement that there be evidence conclusively demonstrating causation of actual harm in specific individuals. In our evaluation . . ., we

> can consider any relevant evidence, including scientific data about the toxicological properties of a dietary ingredient or its mechanisms of action; scientific information about the well-known effects of pharmacologically-related compounds, including those regulated as drugs; to results of clinical studies including observational studies; and adverse event reports that have been subject to sound scientific analysis.

[69 Fed. Reg. at 6817]

> Because it is not reasonable to conclude that a product is too risky in the absence of any significant evidence, *some* weight of evidence of risk is required to meet this standard. For example, isolated adverse events alone might not be expected to constitute substantiation of risk, but adverse event reports combined with pharmacological and other clinical evidence might be expected to do so.

[69 Fed. Reg. at 6788 (emphasis added)]

32. In defining the standard, FDA would consider "only known and reasonably likely benefits, not speculative benefits. A reasonably likely benefit is one that is supported by a meaningful totality of the evidence, given the current state of scientific knowledge, though the evidence need not necessarily meet the approval standard for a prescription drug." [69 Fed. Reg. at 6798]

33. In defining the standard, FDA subjectively down-graded all benefits except those that it found backed by substantial scientific evidence and then refused to extrapolate from that evidence to long-term benefits in the absence of long-term studies:

> We give more weight to benefits that improve health outcomes, especially in the long term, than to benefits that are temporary or rely on subjective measures such as feeling or looking better. For example, sustained, long-term weight loss in an obese or overweight person is a much more important benefit than short-term weight loss because long-term weight loss in those individuals reduces the risk of serious morbidity and mortality (e.g., heart attacks and strokes), while short-term weight loss does not.

[69 Fed. Reg. at 6799]

34. In defining the standard, FDA does not give any weight to benefits that improve health outcomes if those benefits reveal that the dietary supplement cured, mitigated, or treated a disease or disease symptom. That evidence of significant health benefit is excluded from consideration on the theory that, if the supplement were marketed with claims of those effects, the product would be transformed by operation of law into an unapproved new drug. Consequently, FDA refused to consider evidence of the effect of ephedrine alkaloids on the condition of obesity, because FDA has defined obesity as a disease. [See 69 Fed. Reg. at 6795; 6820-6821]

35. In FDA's 2004 Final Rule, FDA did not address Nutraceutical's comments. So, Nutraceutical, on April 20, 2004, for the fourth time requested that FDA exempt its low dose ephedra dietary supplement from the Final Rule. Nutraceutical submitted additional proof that its dietary supplement containing low levels of ephedrine alkaloids was not associated with any serious adverse event and contained ephedrine levels not known to produce any significant adverse effects. [That request is attached as **Exhibit F**] Defendants did not respond to the request.

36. FDA has no scientific evidence from well-designed human clinical trials establishing that ephedrine alkaloids of 10 mg or less per day cause any significant adverse effect. [See Nutraceutical Corp.'s Supplemental Comments & Scientific Report by Michael J. Glade, Ph.D., FACN, CNS, LDN (Apr. 20, 2004); 95N-0304, Sup. 4 (attached as **Exhibit F**)]

37. The daily consumption of 10 mg or less of ephedrine alkaloids is not associated with acute or cumulative adverse effects on the cardiovascular system. [See Nutraceutical Corp.'s Supplemental Comments & Scientific Report by Michael J. Glade,

Ph.D., FACN, CNS, LDN (Apr. 20, 2004); 95N-0304, Sup. 4 (attached as **Exhibit F**)] The 2004 Final Rule is the first time FDA has banned an entire class of dietary ingredients from being sold in the U.S. [See "Remarks by Lester M. Crawford, DVM, Ph.D., Acting Commissioner of FDA for Public Affairs Workshop" (April 19, 2004) at http://www.fda.gov/oc/speeches/2004/aspet0419.html., (attached as **Exhibit G**)]

38. The 2004 Final Rule is the first time FDA presented a risk-benefit comparison standard for determining the existence of food adulteration under the FDCA. [Id]

39. The FDA Commissioner has stated that the risk-benefit comparison standard adopted in the 2004 Final Rule will be applied to evaluate whether dietary supplements containing ingredients other than ephedrine alkaloids are adulterated. [See id]

40. Although FDA, in its 2004 Final Rule, declared adulterated all ephedrine alkaloids, even down to a molecule, when in a dietary supplement, it expressly ruled exempt from its adulteration ruling all ephedrine alkaloids in conventional foods (like ephedra tea) and all ephedrine alkaloids marketed as traditional Asian medicines without a prescription, regardless of the quantity of ephedrine alkaloids:

> This final rule applies to dietary supplements containing ephedrine alkaloids . . . The final rule does not apply to conventional food products that contain ephedrine alkaloids.
>
> Several Ephedra species (including those known as ma huang) have a long history of use in traditional Asian medicine. These products are beyond the scope of this rule because they are not marketed as dietary supplements.

[69 Fed. Reg. at 6793-6794]

41. The administrative record underlying the 2004 Final Rule includes comments explaining the availability of ephedra herb sold as a tea, a food. [See Comments of American Herbal Products Association at 19, 23-24 (Apr. 7, 2003), 95N-0304, C3928 (attached as **Exhibit H**); Ad Hoc Committee on the Safety of Ma Huang, Brief History of Ephedra Concerns and Safety at 2 (Sept. 16, 1996) (attached to Katherine Dearstyne's Comments at 15), 95N-0304, C69(attached as **Exhibit I**)]

42. FDA's own evidence reveals ephedra herb sold as a tea includes per serving amounts of ephedrine alkaloids that range from 15 mg to 30 mgs or more with multiple servings per sitting common. [See e.g., FDA's Briefing Materials for Food Products Containing Ephedrine Alkaloids at 5 (Oct. 11-12, 1995), 95N-0304, Vol. 39, Ref. 1 (attached as **Exhibit J**)]

43. The administrative record underlying the 2004 Final Rule includes comments explaining the availability of ephedra herb in cities of the United States where it is prepared for use in teas and in dietary supplements for ingestion as traditional Asian medicine without a prescription. [See Comments of American Herbal Products Association at 19, 23-24 (Apr. 7, 2003), 95N-0304, C3928 (attached as **Exhibit H**); Comments of California Society for Oriental Medicine at 1 (Aug. 19, 1997), 95N-0304, C1950 (attached as **Exhibit K**); Laraine Crampton's Comments at 1-2 (June 1, 1997), 95N-0304, C408 (attached as **Exhibit L**); Comments of Council of Acupuncture and Oriental Medicine Associations at 3 (Aug. 21, 1997), 95N-0304, C2105 (attached as **Exhibit M**)]

ARGUMENT

Under Fed. R. Civ. P. 56(c), summary judgment shall be granted "if . . . there is no genuine issue as to any material fact and . . . the moving party is entitled to judgment as a matter of law." United States v. Denver, 100 F.3d 1509, 1512 (10th Cir. 1996). A factual dispute is "genuine" if the evidence is such that a reasonable jury could return a verdict for the nonmoving party. Kaul v. Stephan, 83 F.3d 1208, 1212 (10th Cir. 1996). A fact is "material" if it might affect the outcome of the suit under the governing substantive law. Id.

The Court should enter summary judgment in Plaintiffs' favor on Plaintiffs' claims 3 and 4 because there is no genuine issue of material fact, and Plaintiffs are entitled to judgment as a matter of law on those claims.

I. DEFENDANTS VIOLATED THE APA NOTICE-AND-COMMENT REQUIREMENT

A. APA Notice-and-Comment Requirement

Under the APA, agency rules[1] "may be issued only after the familiar notice-and-comment procedures enumerated in the statute are completed." APA Section 553, 5 U.S.C. § 553; Lincoln v. Vigil, 508 U.S. 182, 197n.6 (1993); Comty. Nutrition Inst. et al. v. Young, 818 F.2d 943, 945 (D.C. Cir. 1987); Ballesteros v. Ashcroft, 452 F.3d 1153, 1158 (10th Cir. 2006) ("If a challenged agency action creates a 'legislative rule,' then full compliance with the APA's notice and comment process is required," citing Mission Group Kansas, Inc. v. Riley, 146 F.3d 775, 781 (10th Cir. 1998)); U.S. v. Seward et al., 1981 U.S. App. LEXIS 21300, at 9 n.2 (10th Cir. 1981); id. at 9 ("All legislative or

[1] Agency rules are defined in the APA as "the whole or a part of an agency statement of general or particular applicability and future effect designed to implement, interpret, or prescribe law or policy . . . ," APA Section 551(4), 5 U.S.C. § 551.

substantive rules issued pursuant to a delegation of congressional authority . . . and having the force of law are subject to the requirements of APA § 553 unless otherwise exempt"). The Section 553 notice-and-comment requirement affords "'interested persons an opportunity to participate . . . through submission of written data, views, or arguments,'" Lincoln, 508 U.S. at 195, citing 5 U.S.C. § 553(b),(c).

The fundamental purpose for requiring notice and comment for agency rules has been described concisely by the Tenth Circuit: "The objective of these provisions is not merely notice but also to insure opportunity for debate and mature consideration of the proposal." Seward, 1981 U.S. App. LEXIS 21300, at 9. That purpose was previously articulated by the D.C. Circuit in American Bus. Ass'n v. United States, 627 F.2d 525, 528 (D.C. Cir. 1980):

> The "principal purpose" of section 553 was "to provide that the legislative functions of administrative agencies shall so far as possible be exercised only upon public participation on notice . . . ." [S. Doc. No. 248, 79th Cong., 2d Sess. 244, 257 (1946)] Congress thus selected public participation in rule-making as its means of assuring that an agency's decisions are both informed and responsive. As we have said before, "if the Agency in carrying out its 'essentially legislative task,' has infused the administrative process with the degree of openness, explanation, and participatory democracy required by the APA, it will thereby have 'negate(d) the dangers of arbitrariness and irrationality in the formulation of rules . . . .'" Weyerhaeuser Co. v. Costle, 590 F.2d 1011, 1027-28 (D.C. Cir. 1978).

The notice-and-comment requirement is often said to have two purposes: "'to reintroduce public participation and fairness to affected parties after governmental authority has been delegated to unrepresentative agencies,' American Hosp. Ass'n v. Bowen, 834 F.2d 1037, 1044 (D.C. Cir. 1987) . . . and to assure that the agency is

presented with all information and suggestions relevant to the problem at issue. . ." White v. Shalala, 7 F.3d 296, 303 (2nd Cir. 1993).[2]

Notice-and-comment rulemaking applies to "final" agency action that results in the adoption of "a *de facto* rule or binding norm," NHTSA, 452 F.3d at 806 (D.C. Cir. 2006); Young, 818 F.2d at 946. Agency action creates a *de facto* rule or binding norm if it "mark[s] the 'consummation' of the agency's decision-making process," and it determines "'rights or obligations'" or "'legal consequences . . . flow'" from it. NHTSA, 452 F.3d at 806, citing Bennett v. Spear, 520 U.S. 154, 177-78 (1997); see also Ballesteros, 452 F.3d at 1158, citing Morton v. Ruiz, 415 U.S. 199, 232 (1974) (Legislative rules "affect[] individual rights and obligations").

Notice-and-comment rulemaking applies to an agency's legislative or substantive regulation. Lincoln, 508 U.S. at 196, citing 5 U.S.C. § 553(b); McLouth Steel Products Corp. v. Thomas, 838 F.2d 1317, 1320 (198); Young, 818 F.2d at 945-946 (1987), 950-952 (*per curiam*); and Anthony, Interpretive Rules, Policy Statements, Guidances, Manuals, and the Like – Should Federal Agencies Use Them to Bind the Public?, 41 Duke L. J. 1311, 1321 (1992); Chrysler Corp. v. Brown, 441 U.S. 281, 301 (1979) (noting that this is "the central distinction among agency regulations found in the APA"). Legislative/substantive regulations are ones "issued by an agency pursuant to statutory authority and which implement the statute . . . . Such rules have the force and effect of law." Batterton v. Fancis, 432 U.S. 416, 425 (1977).

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[2] An "affected party" is one "aggrieved by [the] agency action. See Ctr. for Auto Safety and Public Citizen, Inc. v. NHTSA, 452 F.3d 798, 806 (D.C. Cir. 2006)(citing Md. Dep't of Human Res. v. Dep't of Health & Human Servs., 763 F.2d 1441, 1445 n.1 (D.C. Cir. 1985)). As commenters whose request for exemption of ephedrine alkaloids at levels of 10 mg or less per daily dose were denied by the Final Rule, the Plaintiffs are aggrieved.

Stated another way, legislative/substantive rules establish "binding norm[s]." NHTSA, 452 F.3d at 806; see Ballesteros, 452 F.3d at 1159; Fertilizer Institute v. EPA, 935 F.2d 1303, 1307 (D.C. Cir. 1991). A "binding norm" is one that imposes "rights and obligations" and (as to the need for execution of the rule) does not leave "the agency and its decision-makers free to exercise discretion." Id. In determining whether an agency has established a binding norm, courts examine (1) the agency's "own characterization of the action;" (2) "whether the action was published in the Federal Register or the Code of Federal Regulations;" and (3) "whether the action has binding effects on private parties or on the agency." Id.[3]

There is a presumption that all agency rules require publication and comment. Exceptions to publication are disfavored. American Bus. Ass'n, 627 F.2d at 528 ("In sum, as this court said in Humana of South Carolina v. Califano, 590 F.2d 1070, 1082 (D.C. Cir. 1978), '[t]he salutary effect of the Act's public comment procedures cannot be gainsaid, so only reluctantly should courts recognize exemptions therefrom"); see also, Alcaraz v. Block, 746 F.2d 593, 612 (9th Cir. 1984) ("The exceptions to section 553 will

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[3] In contrast to a legislative/substantive rule, an interpretive rule or policy statement is not subject to notice-and-comment rulemaking. An interpretive rule "is a declaration issued without lawmaking authority or without any intent to exercise that authority." As the Tenth Circuit stated in Seward:

> Neither an interpretative rule nor a statement of policy is determinative of the rights or issues it addresses. Pacific Gas & Electric Co. v. FPC, 506 F.2d 33, 37 n.14, 38, 41 (D.C. Cir. 1974). A general policy statement presages an upcoming rule or announces the course an agency intends to follow in future adjudications. Id. at 38. An interpretative rule "does not impose any rights and obligations," Texaco, Inc. v. FPC, 412 F.2d 740, 744 (3d Cir. 1969), and "has no independent binding effect." Eastern Kentucky Welfare Rights Organization v. Simon, 506 F.2d 1278, 1290 (D.C. Cir. 1974), vacated for lack of standing, 426 U.S. 26 (1976).

1981 U.S. App. LEXIS 21300, at 13.

be 'narrowly construed and only reluctantly countenanced[,]' Am. Fed'n of Gov't Employees v. Block, 655 F.2d 1153, 1156 (D.C. Cir. 1981) ("[t]his is consistent . . . with Congress's clear intent to preserve the statutory purpose of informal rulemaking by making sure those exceptions did not become 'escape clauses'"); Nat'l Ass'n of Home Health Agencies v. Schweiker, 690 F.2d 932, 949 (D.C. Cir. 1982) ("Exceptions to the notice and comment provisions . . . are to be recognized 'only reluctantly[;]' [o]therwise, the salutary purposes behind the provisions would be defeated"); Batterton v. Marshall, 648 F.2d 694, 708 (D.C. Cir. 1980) (exemptions from publication "cannot apply . . . . where the agency action trenches on substantive rights and interests").

B. In the 2004 Final Rule, Defendants Adopted a Legislative/Substantive Rule Without Notice-and-Comment

A dietary supplement is defined as a food within the meaning of the Food Drug and Cosmetic Act ("FDCA"), 21 U.S.C. § 321(ff). Prior to the 2004 Final Rule, FDA had never adopted a specific "standard" or test for applying the dietary supplement subpart of the Adulterated Food section of the FDCA. In the 1997 Proposed Rule, FDA, in articulating what it described as its "policy," 62 Fed. Reg. at 30692, assessed adulteration under Section 342(a)(1) and 342(f)(1). It did not assess adulteration under 342(f)(1) alone or under the term "unreasonable" within 342(f)(1) to the exclusion of "significant" within that same subpart. In 21 U.S.C. § 342(a)(1), the FDCA provides:

> A food shall be deemed to be adulterated . . . if it bears or contains any poisonous or deleterious substance which may render it ***injurious to health***; but in case the substance is not an added substance such food shall not be considered adulterated under this clause if the ***quantity*** of such substance in such food does not ordinarily render it ***injurious to health*** . . ."

(Emphasis added). In 21 U.S.C. § 342(f)(1), the FDCA provides:

> A food shall be deemed to be adulterated . . . [i]f it is a dietary supplement or contains a dietary ingredient that . . . presents a ***significant or unreasonable risk of illness or injury*** under conditions of use recommended or suggested in labeling . . .

(Emphasis added).

FDA's proposed adulteration analysis in the 1997 Proposed Rule was based on an amalgamation of the two subparts of 21 U.S.C. § 342, subpart (a)(1), under which "food" substances "injurious to health" are deemed adulterated, and subpart (f)(1), under which "dietary ingredients" and "dietary supplements" that present a "significant or unreasonable risk of illness or injury" are deemed adulterated. That amalgamation, to quote FDA in the 1997 Proposed Rule, was its then existing "policy," 62 Fed. Reg. at 30692. That amalgamation is a reasonable interpretation of the Adulterated Food section because the FDCA, in 21 U.S.C. § 321(ff), defines "dietary supplement" as a food: "a dietary supplement shall be deemed to be a food within the meaning of this Act."

Unlike in its 2004 Final Rule, FDA in its 1997 Proposed Rule did not segregate the "injurious to health" adulteration analysis from the "significant or unreasonable risk" analysis in reaching its tentative conclusion that dietary supplements containing ephedrine alkaloids were adulterated at 8 mg or more per serving. Moreover, it did not evaluate "significant or unreasonable risk" in a disjunctive sense but considered each of the terms "significant" and "unreasonable" as modifying "risk," thus construing them conjunctively. Indeed, unlike in its 2004 Final Rule, FDA in its 1997 Proposed Rule did not provide a definition for "unreasonable" as begetting a standard comparing risks with benefits and as one that could occur without regard to the significance of risk. In the 1997 Proposed Rule, FDA gave no separate definition for "unreasonable." In other

words, FDA in its 1997 Proposed Rule interpreted the entire section as a harmonious whole.

The 1997 Proposed Rule focused on identifying those dose levels that were both injurious to health and that presented a significant and unreasonable risk of illness or injury:

> Based on the available evidence and the likely sources of measurement error around estimated intake levels, the agency tentatively concludes that the use of dietary supplements containing 8 mg or more ephedrine alkaloids per serving may render the dietary supplement ***injurious to health***. The agency also tentatively concludes that consumption of dietary supplements that contain this level or more of ephedrine alkaloids present a ***significant and unreasonable*** risk of illness or injury under the conditions of use recommended or suggested in the labeling or under ordinary conditions of use, and that, therefore, products that contain this or higher levels of ephedrine alkaloids are adulterated.

62 Fed. Reg. at 30693 (emphasis added).

The FDA quoted the two subparts of 21 U.S.C. § 342, subparts (a)(1) and (f)(1) repeatedly, intertwining one with the other. It did so establishing, as does the statute through its union of the two subparts under a single Adulterated Food section, the propriety of this interpretive consolidation based on the fact that a dietary supplement is a food. FDA wrote:

> Under section 402(a)(1) of the act, a food, ***including a dietary supplement***, is adulterated if it bears or contains any added or poisonous or deleterious substance that may render it ***injurious to health***. Section 402(f)(1)(A) of the act provides that a dietary supplement is adulterated if it, or one of its ingredients, poses a ***significant or unreasonable risk of injury or illness*** when used as directed or under ordinary conditions of use. Under section 701(a) of the act, FDA has authority to issue regulations for the efficient enforcement of the act. These sections authorize FDA to issue a regulation that establishes a level of ephedrine alkaloids that, the available evidence makes clear, will render a dietary supplement adulterated as a matter of law.

62 Fed. Reg. at 30693 (emphasis added).[4]

FDA's combined Section 342(a)(1) and Section 342(f)(1) analytical construct presented in the 1997 Proposed Rule is referred to hereinafter as the "Consolidated Standard."

The Consolidated Standard in the 1997 Proposed Rule – what FDA referred to as its existing "policy"-- focused on the dose level at which evidence revealed harm and aimed its ban at that perceived level of risk and above (the proposed ban level consisting of an 8 mg per serving quantity and above). This limit was set *per serving*, not per daily dose. The daily dose level set by FDA in the 1997 Proposed Rule was 24 mg or more. 62 Fed. Reg. at 30695.

In the 2000 Modification, FDA withdrew part (but not all) of its 1997 Proposed Rule.[5] Importantly, however, FDA did not propose any deviation from its Consolidated Standard. It asked for more comment on "safety," consistent with that standard; it did not invite comment on whether FDA should adopt a new standard comparing ephedrine

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[4] In reaching its tentative conclusion in the 1997 Proposed Rule, FDA again interpreted the statutory language "significant or unreasonable" in the conjunctive sense mentioned above and again construed the "injurious to health" section, 21 U.S.C. 342(a)(1), together with the "significant or unreasonable risk" section, 21 U.S.C. 342(f)(1), concluding:

> Eight mg per serving and above represent levels at which the presence of ephedrine alkaloids in a dietary supplement may render the product ***injurious to health and presents a significant and unreasonable risk.***

62 Fed. Reg. at 30693 (emphasis added).

[5] FDA withdrew its quantitative amount determination; its label statement "Do not use this product more than 7 days;" the prohibition on labeling claims encouraging long-term intake; and its proposed warning for short term use. FDA reacted to GAO criticism that FDA's reliance on uncorroborated adverse event reports provided inadequate scientific support for its conclusions. 65 Fed. Reg. at 17474-17475. In the 2000 Modification, FDA referred to risks associated with consumption of dietary supplements containing ephedrine alkaloids and solicited more comment on "safety" of ephedrine alkaloids. 65 Fed. Reg. at 17476.

alkaloid risks with ephedrine alkaloid health benefits as its basis for a finding of adulteration.

In its 2003 Reopened Proposed Rule, FDA expressly reopened the comment period for the 1997 Proposed Rule. "Dietary Supplements Containing Ephedrine Alkaloids; Reopening of the Comment Period," 68 Fed. Reg. 10417 (Mar. 25, 2003). It did not mention, let alone solicit comment on, the adoption of any adulteration standard for dietary supplements other than the existing one, the Consolidated Standard. It did not invite comment on whether FDA should adopt a standard comparing risks of ephedrine alkaloids with their health benefits as a basis for finding adulteration.

Nutraceutical filed comments in response to the 1997 Proposed Rule and in response to the 2003 Reopened Proposed Rule. See Exhibits B and C.

In its 2004 Final Rule, FDA adopted, to use its terms, a "standard" for the "first time" interpreting the "significant or unreasonable risk" subpart of the Adulterated Food section without regard to the decisional factors presented in its 1997 Proposed Rule. 69 Fed. Reg. at 6794 ("we are articulating a standard for unreasonable risk under 402(f)(1)(A) for the first time"). FDA adopted the new standard (1) without regard to the "injurious to health" subpart of 21 U.S.C. § 342; (2) without giving any meaning to the term "significant" risk in subpart 342(f)(1); and (3) without making the ***presence*** of scientific evidence of harm at a particular dose requisite to a determination of risk (but instead holding the ***absence*** of proof of safety at low doses sufficient to support a determination of risk at those doses). The 2004 Final Rule departed strikingly from the 1997 Proposed Rule in its adoption of a new standard for evaluating dietary supplement adulteration.

For the "first time," FDA in its 2004 Final Rule announced that a determination of dietary supplement adulteration would depend on a comparison of risks with health benefits along the following lines: "In the absence of a sufficient [health] benefit, the presence of even a relatively small risk of an important adverse health effect to a user may be unreasonable" ("Risk-Benefit Standard"). 69 Fed. Reg. at 6788. The standard adopted was an interpretation of "unreasonable risk," to the exclusion of "significant risk." The risk side of the standard required little from FDA to meet its burden; the health benefit side required significant evidence to establish a benefit capable of counterweighing any perceived risk. FDA wrote that its burden under the new standard could "be met with any science-based evidence of risk and does not require a showing that the substance has actually caused harm . . ." By contrast, for a benefit to be sufficient to counterweigh risk, it needed to concern long-term improvements in health outcomes established by generally accepted scientific evidence.[6]

FDA, repeatedly in the 2004 Final Rule, describes the Risk-Benefit Standard as a "standard." 62 Fed. Reg. at 6795. It likewise repeatedly describes the Risk-Benefit Standard as its interpretation for the "first time" of the statutory term "unreasonable" in 21 U.S.C. 342(f)(1), 62 Fed. Reg. 6794. FDA applied the standard to all ephedrine alkaloid containing dietary supplements and banned them all. 62 Fed. Reg. 6793.

[6] The benefit had to be "known and reasonably likely" with a "reasonably likely benefit" constituting one that "is supported by a meaningful totality of the evidence, given the current state of scientific knowledge, though the evidence need not necessarily meet the approval standard for a prescription drug." 62 Fed. Reg. at 6798.

C. The Risk-Benefit Standard Is a Legislative/Substantive Rule

The Risk-Benefit Standard is a legislative/substantive rule that could not have been legally adopted except by following the familiar notice-and-comment procedures of the APA. 5 U.S.C. § 553. FDA failed to follow those required procedures.

The Risk-Benefit Standard without question is a final rule. It establishes a binding norm on the regulated class. It "mark[s] the 'consummation of the agency's decisionmaking process." NHTSA, 452 F.3d at 806. Legal consequences, namely the determination that all dietary supplements containing ephedrine alkaloids are adulterated and illegal for sale, "flow" from it. NHTSA, 452 F.3d at 806. Like the agency rule involved in the 10th Circuit's Seward decision, 1981 U.S. App. LEXIS 21300, at 13, the Risk-Benefit Standard is determinative of the rights and issues before the agency. The Risk-Benefit Standard bans all ephedrine alkaloids from dietary supplements in the United States and, according to the FDA Commissioner, will be applied to ban other ingredients from dietary supplements. See "Remarks by Lester M. Crawford, DVM, Ph.D., Acting Commissioner of FDA for Public Affairs Workshop" (April 19, 2004) at http://www.fda.gov/oc/speeches/2004/aspet0419.html (**Exhibit G**). It fixes the rights and obligations of Nutraceutical and all similarly situated by denying Nutraceutical and those others the freedom to sell dietary supplements containing ephedrine alkaloids. It fixes the rights and obligations of the entire dietary supplement industry by establishing a new adulteration standard to govern all dietary supplement ingredients.

The Risk-Benefit Standard undeniably is a legislative/substantive rule. It is a radical departure from the law pre-existing the 2004 Final Rule. The Risk-Benefit Standard is a startlingly complete substantive break with the Consolidated Standard. The

Risk-Benefit Standard is not a logical outgrowth of the Consolidated Standard. The Risk-Benefit Standard is not "in 'character with the original scheme'" presented in the 1997 Proposed Rule, and is not "foreshadowed" by the Consolidated Standard. Cf. Beirne v. Secretary of Department of Agriculture, 645 F.2d 862, 865 (10th Cir. 1981). The Consolidated Standard is based on the food and the dietary supplement subparts of 21 U.S.C. § 342 combined; the Risk-Benefit Standard is based on the dietary supplement subpart alone and only on the "unreasonable risk" language within that statutory subpart to the exclusion of the "significant risk" language. The Consolidated Standard identified that quantity of ephedrine alkaloids that produce harm and banned ephedrine alkaloids at that level and above; the Risk-Benefit Standard compares even slight risk with known and reasonably likely health benefits and deems that comparison to result in a finding of adulteration at all dose levels. The Consolidated Standard was based on FDA's then existing "policy" amalgamating section 342(a)(1)("injurious to health") with 342 (f)(1)("significant or unreasonable risk") to form a unified food adulteration standard; the Risk-Benefit Standard is entirely new and applies only to dietary supplements, not to foods in general.

D. The 2004 Final Rule is Invalid Because FDA Failed to Comply With the APA's Notice-and-Comment Requirement

Nutraceutical was caught entirely by surprise when the 2004 Final Rule included a "first time" ever standard for determining dietary supplement adulteration separate, apart, and entirely different from the Consolidated Standard in the 1994 Proposed Rule. If Plaintiffs had known that the Risk-Benefit Standard was in the offing, they would have commented at length about it and would have advised the agency on alternative standards and alternative constructs that would, in their judgment, better serve to protect the public,

ensure consistency in the interpretation of 21 U.S.C. § 342, and ensure stability in the industry. See the Affidavit of Nutraceutical's Executive Vice President and Chief Operating Officer Jeffrey A. Hinrichs attached as **Exhibit E**. Plaintiffs were unlawfully denied that opportunity by the FDA.

FDA was required by the APA to publish notice of the Risk-Benefit Standard and afford the public, including the plaintiffs, an opportunity to comment upon it. See Buschmann v. Schweiker, 676 F.2d 3521, 355-56 (9th Cir. 1982) (Agency rules are invalid if the agency fails to comply with the APA requirements); Chrysler Corp., 441 U.S. at 313 ("certainly regulations subject to the APA cannot be afforded the 'force and effect of law' if not promulgated pursuant to the statutory procedural minimum found in that Act"); Linoz v. Heckler, 800 F.2d 871, 878 (9th Cir. 1986). FDA failed its basic and irreducible duty and, by so doing, defeated the central purpose the Tenth Circuit recognized for the APA notice-and-comment provision: it denied all who would comment their statutory right to notice and it also failed "to insure opportunity for debate and mature consideration of the proposal." Seward, 1981 U.S. App. LEXIS 21300, at 9; see also Morton v. Ruiz, 415 U.S. at 232 ("The Administrative Procedure Act was adopted to provide, *inter alia*, that administrative policies affecting individual rights and obligations be promulgated pursuant to certain stated procedures so as to avoid the inherently arbitrary nature of unpublished *ad hoc* determinations. See generally S. Rep. No. 752, 79th Cong., 1st Sess., 12-13 (1945); H. R. Rep. No. 1980, 79th Cong., 2d Sess, 21-23 (1946)"); American Bus. Ass'n v. United States, 627 F.2d 525, 528 (D.C. Cir. 1980) ("'. . .the law must provide that . . . the regulators shall be regulated, if our present

form of government is to endure,' quoting S. Doc. No. 248, 79th Cong., 2d Sess. 244 (1946), quoting H.R. Rep. No. 1149, 76th Cong., 1st Sess. 2 (1939)").

This Court, based on FDA's violation of the APA, should declare that the Defendants' violation of the APA's notice-and-comment requirements renders the 2004 Final Rule invalid. In addition, because the 2004 Final Rule's Risk-Benefit Standard is its *sine qua non*, the Court should also remand the rule to the FDA and require the agency to reopen the rulemaking and accept comment on its proposed Risk-Benefit Standard.

II. THE 2004 FINAL RULE VIOLATES THE APA PROHIBITION ON ARBITRARY AND CAPRICIOUS DECISION-MAKING

Under the APA, agency rules are "unlawful," and hence void, if they are "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A). Whether an agency acted in an arbitrary and capricious manner is determined by whether the agency's decision was based on a consideration of all the relevant factors and whether it has made a clear error of judgment. Citizens to Preserve Overton Park, Inc. v. Volpe, 401 U.S. 402, 416 (1971). An agency decision will be considered arbitrary and capricious if the agency "entirely failed to consider an important aspect of the problem, offered an explanation for its decision that runs counter to the evidence before the agency, or is so implausible that it could not be ascribed to a difference in view or the product of agency expertise." Motor Vehicle Mfrs. Ass'n v. State Farm Mutual Auto. Ins. Co., 463 U.S. 29, 43 (1983) (emphasis added); see also, Humana of Aurora v. Heckler, 753 F.2d 1579, 1581 (10th Cir. 1985) (citations omitted). "A rational connection must be found between the facts before the agency and the rule-making choice made." Id. (citing Motor Vehicle Mfrs., 463 U.S. 29); see also, Burlington Truck Lines v. U.S., 371 U.S. 156, 168 (1962).

The 2004 Final Rule is irrational and internally inconsistent. FDA declared in its 2004 Final Rule that all ephedrine alkaloids, even down to a molecule, were adulterated when in a dietary supplement, but, in stark contrast, simultaneously declared that ephedrine alkaloids in conventional foods (like ephedra tea) and in traditional Asian medicine sold without a prescription were exempt from its ban, regardless of the quantity or dose. 69 Fed. Reg. at 6793-6794, 6814. The 2004 Final Rule renders regulation to achieve public health objectives incoherent, depending on the form of presentation of the substance said to be toxic, not on the substance itself. It defeats the purpose of the Adulterated Food section of the Act by rendering that section internally inconsistent, preventing achievement not only of the goal of that section but also of the avowed objective of the rule itself: protection of public health. It makes no rational scientific sense for a microgram of ephedrine to be illegal in a supplement but for every amount to be exempt from the ban when in the very same product relabeled traditional Asian medicine or when in a conventional food, such as ephedra tea.

The point is exacerbated in the context of this case because Plaintiffs' raw crushed *Ephedra sinica* herb is exactly the same substance sold as ephedra tea. See *supra* Statement of Uncontested Material Facts at paragraphs 2, 4. Thus, Plaintiffs are barred by the 2004 Final Rule from placing their raw crushed *Ephedra sinica* herb in a gelatin capsule and selling it as a dietary supplement, but are exempt from the 2004 Final Rule if they sell that very same herb as a tea, regardless of per serving amount. To borrow Jeremy Bentham's apt phrase from another context, this is "nonsense upon stilts."[7] Indeed, as FDA's own record establishes, ephedra teas commonly cause those

[7] See Jeremy Bentham, 'Nonsense Upon Stilts' in Philip Schofield, Catherine Pease-Watkin & Cyprian Blamires, *Rights, Representation and Reform: Nonsense Upon Stilts and Other Writings on the French Revolution* 364 (Oxford, 2002).

who consume them to ingest between 15 and 30 mg or more of ephedrine alkaloids per serving (with multiple servings common among tea drinkers in a single sitting). See e.g., FDA's Briefing Materials for Food Products Containing Ephedrine Alkaloids at 5 (Oct. 11-12, 1995), 95N-0304, Vol. 39, Ref. 1 (**Exhibit J**). The rule thereby turns not on the food *substance* but on the food *form* and makes a mockery of, even defeats and undermines, public health policy under the FDCA's Adulterated Food section. There is, in short, no rational connection between the decision that ephedrine alkaloids are adulterated down to a molecule in dietary supplements, and the 2004 Final Rule exemption from adulteration given all ephedrine alkaloid containing conventional foods and all ephedrine alkaloid containing traditional Asian medicines sold without a prescription.

The 2004 Final Rule establishes an arbitrary and capricious standard, not only in the context of ephedra, but in every other context in which the rule will be applied. By definition, a dietary supplement is a food and, in particular, is often comprised of constituent elements of foods (vitamins, minerals, amino acids, herbs). See 21 U.S.C. § 321(ff)(1). Consequently, the application of the Risk-Benefit Standard exclusively to supplements without regard to foods containing the same ingredients ensures in every case that it will produce over-inclusive and under-inclusive decision-making that is patently irrational and inconsistent. The standard is under-inclusive in every case because its limitation to the dietary supplement context ensures that foods containing the same substances banned will remain exempt from the ban. The standard is over-inclusive in every case because its implementation bans a dietary ingredient without regard to the presence of scientific proof of harm, discriminating against supplements in

favor of foods that may contain, as here, dose amounts that exceed the level at which scientific evidence reveals harm.

For the foregoing reasons, the 2004 Final Rule is arbitrary and capricious within the meaning of the APA, 5 U.S.C. § 706(2)(A), and should therefore be declared invalid.

III. THE COURT SHOULD ENJOIN THE DEFENDANTS FROM ENFORCING THE UNLAWFUL 2004 FINAL RULE

The 2004 Final Rule violates the Administrative Procedure Act and is therefore unlawful. An injunction is commonly granted where an exclusive business has been invaded and where it is shown that an irreparable injury has been inflicted. See Vaughan v. John C. Winston Co., 83 F.2d 370 (10th Cir. 1936). An injunction is commonly granted against enforcement of a rule when it is held to be in violation of the APA. See e.g., Webster v. Doe, 486 U.S. 592, 599-605 (1988) (remanding to federal district court for consideration of APA injunctive relief claim). Where it is determined that an adequate remedy at law is lacking, monetary damages would be difficult and perhaps impossible to ascertain, or the invaded business would be forced to bring a series of successive lawsuits for damages to repair the irreparable injury, an injunction will be granted. Vaughan, 83 F.2d at 374.

In this case, FDA's 2004 Final Rule is invalid for the reasons explained above, and plaintiffs have been irreparably harmed by the 2004 Final Rule, which has destroyed the entire ephedra dietary supplement marketplace in the United States, including plaintiffs' ephedrine alkaloid containing dietary supplement business. Therefore, the Court should enjoin Defendants from enforcing their 2004 Final Rule and compel Defendants to reopen the rulemaking in question and serve notice and provide an opportunity to comment to the regulated class. Defendants should also be compelled to

issue a new ultimate decision consistent with the decision of this Court and, in particular, one that will treat ephedrine alkaloids in foods and in traditional Asian medicines sold without a prescription the same as in dietary supplements.

IV. CONCLUSION

For the foregoing reasons, Plaintiffs respectfully request that this Honorable Court declare the Final Rule invalid in violation of the Administrative Procedure Act, 5 U.S.C. §§ 553 and 706; remand the matter to the agency for further rulemaking consistent with the Court's opinion; and enjoin the Defendants from enforcing the 2004 Final Rule.

Dated this 20th day of December, 2006.

Respectfully submitted,

SOLARAY, INC. AND
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CERTIFICATE OF SERVICE

I hereby certify that on this ___ day of December, 2006, I electronically filed a true and correct copy of the foregoing MEMORANDUM OF POINTS AND AUTHORITIES IN SUPPORT OF PLAINTIFFS' MOTION FOR SUMMARY JUDGMENT with the Clerk of the Court using the CM/ECF system which sent notification of such filing to the following:

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